Unveiling visionary frontiers: a survey of cutting-edge techniques in deep learning for retinal disease diagnosis

Rajatha[1,2], Ashoka Davanageri Virupakshappa[3]
[1]Department of Computer Science and Engineering, JSS Academy of Technical Education, Bengaluru, Visvesvaraya Technological University, Belagavi, India
[2]Department of Computer Science and Engineering, RV College of Engineering, Bengaluru, India
[3]Department of Information Science and Engineering, JSS Academy of Technical Education, Bengaluru, Visvesvaraya Technological University, Belagavi, India

Article Info

Article history:

Received Nov 7, 2023
Revised Dec 25, 2023
Accepted Dec 1, 2023

Keywords:

Age-related macular disease
Convolutional neural network
Diabetic retinopathy
Ensemble learning
Glaucoma screening
Multi-label classification
Transfer learning

ABSTRACT

Retinal disorders impact millions of people globally. These disorders can be detected and diagnosed early enough to not only cure but also avoid permanent blindness. Manual identification of these diseases has always been tedious, time-consuming, and inconsistent. For ophthalmologists, retinal fundus images are a valuable source of information in diagnosing retinal diseases. Automatic identification of eye disorders using artificial intelligence (AI) based learning models has seen substantial development in the computer vision sector recently. Various models, particularly deep learning (DL) models are incredible in identifying and classifying diseases. In the presented review, we have performed an in-depth analysis of various existing DL models, involving preprocessing, classification, segmentation, and techniques to deal with data imbalance. We have also endeavored to gauge the effectiveness of these models by evaluating their performance using the metrics employed in their assessment. In addition, we explored various challenges along with the potential future scope in this domain.

This is an open access article under the CC BY-SA license.

Corresponding Author:

Rajatha
Department of Computer Science and Engineering, Visvesvaraya Technological University
Belagavi, India
Email: rajathabhatkaje@gmail.com

1. INTRODUCTION

According to current estimates, there are approximately 2.2 billion individuals suffering from visual impairments across the globe. At least 1 billion of these cases could have been averted or whose causes have not yet been addressed, per the World Health Organization (WHO) [1]. The major causes of these diseases are attributed to ocular diseases. Vision loss and blindness have significant adverse social and psychological effects in all societies. Medical imaging is evolving rapidly and has a substantial impact on patient management today. The precise and timely diagnostics by this imaging technique have shown promising results in visualizing anomalies existing in the patient's body, determining disease stages, progression, and treatment planning. For instance, in ophthalmology, the availability of optical coherence tomography (OCT) is unparalleled. It has reduced the dependency on ophthalmologists' expertise and knowledge. Examining and grading the images manually is not just cumbersome and laborious; it could also lead to misinterpretation and the waste of health data. However, with the increasing volume and complexities of medical diagnostic imaging, interpretation and controlling retinal disease is more complicated due to the diverse images and findings that are recorded for individuals, and also the hypothesis that supports it [2].

While conventional diagnostic techniques were heavily based on the physician's ability to manually assess the medical data, modern clinical diagnostic techniques rely on intelligent technologies to manage the medical data efficiently. Computer-aided diagnosis (CAD) and other artificial intelligence (AI) disciplines have proven to be highly productive in screening seemingly huge-scale data [2], [3]. Furthermore, AI has a substantial role in the field of ophthalmology, especially in diagnosis and therapy for retinal diseases because of its practical image interpretation [3], [4]. Retinal diseases vary widely based on categories and disease phases. Early detection is crucial for curable diseases, as overlooking them can lead to gradual vision loss and permanent blindness. Common retina diseases include diabetic retinopathy (DR), cataracts, glaucoma, age-related macular degeneration (AMD), retinal detachment, retinal tear, and macular hole. Limited clinical data availability makes refining the accuracy of medical imaging modalities challenging. However, with the advent of deep learning (DL), automated diagnosis of multiple retinal ailments has gained significant interest.

The study's remaining sections are structured as follows: Section 2 delves into the transition from traditional machine learning (ML) to DL, exploring various CNN models. Transfer learning, Multi-label classification, and Ensemble approaches are covered in Sections 3, 4, and 5, respectively. Section 6 addresses data imbalance through data augmentation techniques. Section 7 critically examines DL techniques, their performances, and vulnerabilities. The paper concludes in Section 8.

2. OUTLINE OF DL METHODS

A class of AI called ML trains the system to gain knowledge from the chunk of data, followed by accurate predictions without much human interference. It can further be classified as supervised, unsupervised, and reinforcement learning [5]-[9]. The conventional ML algorithms are shown in Table 1.

According to current estimates, there are approximately 2.2 billion individuals suffering from visual impairments across the globe. At least 1 billion of these cases could have been averted or whose causes have not yet been addressed, per the WHO [1]. The major causes of these diseases are attributed to ocular diseases. Vision loss and blindness have significant adverse social and psychological effects in all societies. Medical imaging is evolving rapidly and has a substantial impact on patient management today. The precise and timely diagnostics by this imaging technique have shown promising results in visualizing anomalies existing in the patient's body, determining disease stages, progression, and treatment planning. For instance, in ophthalmology, the availability of OCT is unparalleled. It has reduced the dependency on ophthalmologists' expertise and knowledge. Examining and grading the images manually is not just cumbersome and laborious; it could also lead to misinterpretation and the waste of health data. However, with the increasing volume and complexities of medical diagnostic imaging, interpretation and controlling retinal disease is more complicated due to the diverse images and findings that are recorded for individuals, and also the hypothesis that supports it [2].

While conventional diagnostic techniques were heavily based on the physician's ability to manually assess the medical data, modern clinical diagnostic techniques rely on intelligent technologies to manage the medical data efficiently. CAD and other AI disciplines have proven to be highly productive in screening seemingly huge-scale data [2], [3]. Furthermore, AI has a substantial role in the field of ophthalmology, especially in diagnosis and therapy for retinal diseases because of its practical image interpretation [3], [4]. Retinal diseases vary widely based on categories and disease phases. Early detection is crucial for curable diseases, as overlooking them can lead to gradual vision loss and permanent blindness. Common retina diseases include DR, cataracts, glaucoma, AMD, retinal detachment, retinal tear, and macular hole. Limited clinical data availability makes refining the accuracy of medical imaging modalities challenging. However, with the advent of DL, automated diagnosis of multiple retinal ailments has gained significant interest.

The study's remaining sections are structured as follows: Section 2 delves into the transition from traditional ML to DL, exploring various CNN models. Transfer learning, multi-label classification, and Ensemble approaches are covered in sections 3, 4, and 5, respectively. Section 6 addresses data imbalance through data augmentation techniques. Section 7 critically examines DL techniques, their performances, and vulnerabilities. The paper concludes in section 8.

Table 1. Classification of ML techniques

Classification	Description	Applications	Algorithms
Supervised learning	The system is trained with labeled datasets	Classification, regression, and forecasting	Linear Classifiers, SVM, Random Forest, Decision Tree, Logistic Regression, KNN, Naive Bayes
Unsupervised learning	The system is provided with datasets that aren't precisely labeled	Clustering and Dimensionality Reduction	k-means, PCA, Hierarchical clustering, Mean Shift
Reinforcement learning	Intelligent agent acquires behavior in an uncertain, complex environment through trial-and-error mechanism	Modeling non-linear relationships in high dimensional data	ANN, Markov Decision Process, Q-learning, Temporal difference learning

High-resolution images are crucial for disease identification and diagnosis applications. Conventional ML algorithms are inadequate due to the unpredictable traits of medical images. Their manual feature selection process and susceptibility to errors from overfitting/underfitting training datasets further hinder accurate predictions [8]. Among the techniques involving medical imaging, the one that has seen a breakthrough in recent years is DL. The major inspiration for DL, a subset of ML that resembles the structure of a human neuron, is the connectivity between neurons in the brain. The deep neural network comprises artificial neural nodes, organized into three layers: an input layer, multiple hidden layers, and an output layer, as illustrated in Figure 1. DL algorithms are capable of performing automatic feature extraction from large data sets to provide accurate results. Numerous DL techniques are available [10], [11] as depicted in the Table 2.

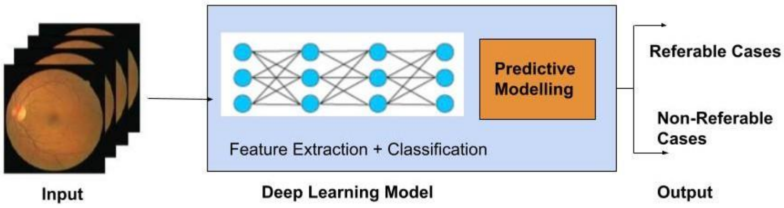
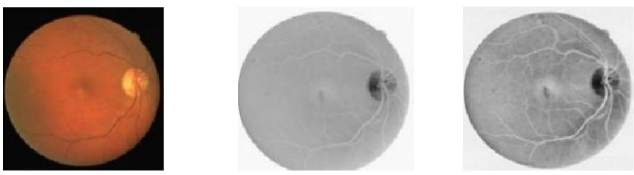


Figure 1. Architecture of deep neural network

Table 2. Classification of DL techniques

Classification	Description	Applications
Deep belief networks	Machines are trained using labeled training data	Classification, regression, recognition, and forecasting
Convolution neural network	Machine analyses and cluster unidentified patterns without human intervention	Clustering and dimensionality reduction
Deep autoencoder	Machines are trained to analyze optimal behavior in their environment to make suitable decisions	Modeling non-linear relationships in high-dimensional data
Deep boltzmann Machine	Extension of RNN, additionally hidden layers and directionless connections between its nodes	Dimension reduction, categorization, regression, collaborative filtering, feature learning
Multi-layer Perceptron (MLP)	MLP has layers of activation-function equipped perceptions	Software for machine translation, image, and voice recognition
Radial basis Functions (RBFs)	RBFs are neural network activation used in RBFNs	Regression, categorization, timeseries forecast

Assessing retinal illness severity relies on fundus datasets, but the raw image quality often lacks precision for minor changes. Noise removal, a critical initial step in fundus image processing, involves applying filters like mean, median, Gaussian, and Wiener to address image imperfections [12], [13]. Enhancing fundus images for precise detection of subtle variations in the retinal vasculature or advanced disease detection requires overcoming challenges like varying vessel lengths, branches, low contrast, and vessel crossings. In the Figure 2, the contrast enhancement comparison with respect to HE as shown in Figure 2(a), AHE as shown in Figure 2(b), and CLAHE as shown in Figure 2(c) is clearly depicted. CLAHE has gained popularity for effectively enhancing contrast in retinal vessels. It surpasses both AHE and conventional HE making it the preferred choice for performance improvement [14]–[19].



(a) (b) (c)

Figure 2. Comparison of contrast enhancement using HE, AHE, and CLAHE: (a) histogram equalization (HE), (b) adaptive histogram equalization (AHE), and (c) contrast limited adaptive histogram equalisation [20]

Various techniques employing CLAHE, involving top-hat and high-boost filters like Butterworth, Frangi, etc were used to eliminate Gaussian, salt-pepper noise and strengthen the red, green, and blue channels [20]–[23]. Techniques involving modified particle swarm optimization (MPSO), a fully attention-based network (FANet) were used on CLAHE to limit intra-class inconsistencies and improve segmentation results [24] A unique fundus image quality assessment and segmentation of OD using CNN and Grab cut algorithm was introduced. The model achieved an accuracy of 98.72%, 99.21%, and 96.43% on DRION, DRISHTI-GS, and RIM-ONE datasets respectively [25].

In the realm of DL, convolutional neural networks (CNNs) stand out significantly, particularly in applications related to computer vision. CNN architecture as shown in Figure 3, consists of input layers for image data, followed by convolutional layers that extract features. Pooling layers reduce spatial dimensions, and fully connected layers perform classification. ReLU activation functions introduce non-linearity, aiding in feature learning. CNNs excel in tasks like image recognition due to their hierarchical feature extraction [26]–[31]. Figure 3 depicts the standard framework of a Deep CNN model.

Liao *et al.* [32] proposed EAMNet, an interpretable model for efficient glaucoma diagnosis. EAMNet includes a CNN backbone for feature extraction, multi-layer average pooling (M-LAP) for connecting semantic and location information, and evidence activation mapping for detection and identification. It achieved an accuracy of 0.88, surpassing contemporary diagnostic techniques. Kou *et al.* [33] suggested an enhanced residual U-Net (ERUNet), for the segmentation of Microaneurysms (MA) and Exudates (EX). ERU-Net generates three U-paths, each made up of three up-sampling paths and one down-sampling path. ERU-Net improves the associated feature fusion and captures the nuances of fundus images with its three U-path structures. Bilal *et al.* [34] introduced a mixed model for DR grading. Three classifiers were used in the classification phase: A model combining support vector machine (SVM), k-nearest neighbor (KNN), and binary tree (BT) models, along with a majority voting method to acquire the final output. Multiple diagnoses from disease grading databases were employed to complete this project, which led to an accuracy of 98.06%, sensitivity of 83.67%, and specificity of 100%. Islam *et al.* [35] developed a multi-stage CNN-based system called DiaNet based on a pre-trained CNN model on ImageNet to diagnose diabetes mellitus.

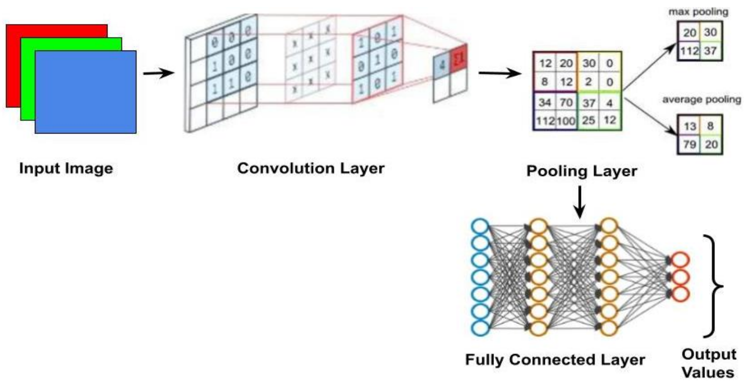


Figure 3. Architecture of a typical deep convolutional neural network

Additional layers were inserted to improve its ability to recognize more complicated patterns in the input. The model is primarily finetuned for DR identification. DiaNet uses Dense-Net as its base CNN and performs multistage fine-tuning to provide a high degree of accuracy of 84.4%. Xu *et al.* [36] introduced a global-local attention network (GLA-net) to tackle the classification of cataracts. The system proposes two subnet levels, global-level attention emphasizes global structure information, and local attention network focuses on discriminative features of specific regions. The model achieved a detection accuracy of 90.65%, grading accuracy of 83.47% and classification accuracy of 81.11%. Zamani *et al.* [37] observed the lack of extensive analysis in the field of pterygium identification using DL and proposed a new framework, VggNet16-wbn, a CNN-based trained network obtained from VggNet16. A network analysis of six pre-trained CNN networks to recognize pterygium led to the presentation of a new CNN-based network architecture. Moosawi and Khudeyer [38] proposed ResNet-n\DR by modifying and adding three residual units to Resnet-34. The proposed model achieved 93.5% accuracy, 90.7% sensitivity, 98.2% specificity, 90.1% F1 score, and 89.5% precision on APTOS-2019 dataset. For maximum performance, DL approaches require large-scale databases to be implemented. Because of data-acquisition elements and other needs, acquiring large-scale images or datasets in various domains, particularly in medical imaging, is a challenging and time-consuming operation.

3. TRANSFER LEARNING

Transfer learning (TL) is a standard technique that is comparable to DL in computer vision as well as natural language processing (NLP) jobs [39]. The foundation of the image classification problem comprehends the training, validation, and testing phases of DL algorithms. The DNN training procedure can be carried out with either new or existing CNN-trained networks as training datasets. Learning from scratch requires a manual network to be built and the structure of DNN to be clearly understood [40]–[42]. Additionally, a large volume of data sets is required. TL is an alternative to training data from the outset, which necessitates large-scale data, for compact data representations in DL [43]. Jabbar *et al.* [44] introduced a VGG-16-based TL model to enhance the classification performance of DR. The model was trained using EyePACS and Kaggle datasets. The model achieved an accuracy of 96.61% which was way higher than the accuracies of ResNet, AlexNet, and GoogleNet. Alghamdi and Mottalebet [45] proposed an automatic glaucoma diagnosis framework using three CNN models— Transfer CNN (TCNN), semi-supervised CNN with self-learning (SSCNN), and semi-supervised CNN with autoencoder (SSCNN-DAE). TCNN transfers knowledge from VGG-16 to a small dataset, SSCNN uses self-learning, and SSCNN-DAE employs a denoising autoencoder for feature extraction. Results show SSCNN-DAE outperformed TCNN and SSCNN, achieving accuracy rates of 93.8%, 91.5%, and 92.4%, respectively.

4. MULTI-LABEL CLASSIFICATION

Multi-label classification (MLC) is regarded as a prominent topic in the research field, especially in the world of computer vision, particularly medical imaging analysis. In MLC, an object can be classified into more than one class. There is no restriction on the number of labels a subject could be assigned in the multi-label problem. We use a range of multi-label classification-specific methodologies to overcome these challenges:

a) Problem transformation: It is the way of transforming a multi-label dataset into a single-label dataset. Machine-readable single-label datasets make it easier to create models. The following techniques are used to transform problems:
- Binary relevance: This technique considers every label independently, and MLC is used to separate them.
- Classifier chain: It is a sequential process in which one classifier output is used as the input for the next classifier in the chain.
- Label power set: It changes the problem to a multi-class problem. The unique label combinations found in the data are then used to train each multi-class classifier.

b) Adapted algorithms: This technique uses the algorithm adaption method to perform MLC.

c) Ensemble model: This is a hybrid method that combines the capabilities of both the above techniques.

Abdelmaksoud *et al.* [46] proposed a multi-label CAD system for detecting and diagnosing DR. The system standardizes retinal image sizes, utilizes GLRLM to extract texture features from pre-processed fundus images, and employs U-Net for automatic detection of exudates, MA, haemorrhages, and blood vessels. Six features are extracted, and a classifier chain ML-SVM is employed to distinguish between different DR grades. Fu *et al.* [47] presented M-Net, a one-stage multilabel system for optic disk (OD) and optic cup (OC) segmentation. M-Net incorporates a U-shaped CNN, multi-scale input layer, side-output layer, and a multilabel loss function. The input layer generates a pyramid representation for various receptive field sizes, and a U-Net model trains the hierarchy structure. The side-output layer acts as an initial classifier, providing local forecast maps for different scale layers. A multi-label loss function yields the final segmentation map, and polar transformation enhances segmentation performance by providing an image depiction in polar coordinates. The system demonstrated satisfactory performance in glaucoma screening on ORIGA and SCES datasets during testing.

Lin *et al.* [48] proposed two MLC schemes: MCG-Net, using graph convolutional networks, and MCGS-Net, combining graph convolutional networks with self-supervised learning. MCG-Net-GCN captures crucial information from multi-label fundus images, while MCGS-Net enhances classification with self-supervised learning. Tested on ODIR and SSL datasets, both demonstrated superior categorization, achieving a 4.74% boost in recall. MCGS-Net exhibits stronger generalization, especially for unseen fundus picture collections. Wang *et al.* [49] introduced Efficient-Net for precise identification of fundus abnormalities in retinal images. It comprises a feature extraction network that scales depths, widths, and resolutions efficiently. The second component is an ML classification neural network with a unique structure. The final classification result is obtained by blending outcome probabilities from various models. Training and testing were conducted using the ODIR 2019 dataset, showing superior outcomes even when trained on fewer datasets [49]. Using MLC and a graph convolutional network (GCN), this model identified eight fundus lesion types in color images.

It consists of a CNN-based Res-Net-101 for image feature extraction and a GCN for classification, utilizing matrices from label embeddings and co-occurrence patterns. The model accurately recognized various lesions, including hemorrhages, laser scars, retinal arteriosclerosis, micro-aneurysms, and hard/soft exudates [50]. MLC-driven gradient-weighted class activation mapping (Grad-CAM) was developed by Jiang *et al.* [51] and it could classify and automatically detect the DR regions with different lesions. First, DR lesions were used as labels for the collection of additional learning data. Second, lesion identification was accomplished by combining Grad-CAM and multi-label classification. They formed a Res-Net-based DL model and achieved 94.4% specificity and 93.9% sensitivity.

5. ENSEMBLE LEARNING

The fundamental idea behind ensemble methods is a linear combination of numerous model-fitting approaches as opposed to only using single-fit. Ensemble learning includes various learning models to achieve better predictive performance than a single model. Ensemble methodologies are broadly classified as Homogeneous Ensemble approaches, involving Bagging and Boosting, Heterogenous Ensemble approaches involving Stacking, and Majority voting algorithms [52]–[55].

- BAGGing: This technique creates an ensemble model through aggregation and bootstrapping, adapting similar learners to small sample populations and using majority voting to combine predictions.
- Boosting: An iterative method aimed at reducing bias error, boosting builds a robust predictive model by adjusting the weights of previous classifications, though it may lead to overfitting.
- Stacking: This method optimally combines predictions from diverse high-performing ML models.
- Majority voting algorithm: Enhancing efficiency through voting, this method determines the final prediction based on the majority vote from each learning algorithm [52], [54].

To enhance the model's prediction, Qummar *et al.* [56] suggested a combination of five DCNN models (Resnet50, Inception-v3, Xception, Dense121, and Dense169) are trained to classify different DR stages by encoding the rich information. Lyu *et al.* [57] proposed a training method for categorizing multiple labels with varying sample sizes and difficulty levels. They calculate inverse frequencies for each category to guide model training. The model is iteratively trained with adjusted class weights, addressing flaws and emphasizing challenging samples. Experimental results from RIADD-2021 yielded an 88.24% accuracy [57].

6. DATA AUGMENTATION TECHNIQUES

The scarcity of substantial, freely available retinal image datasets has been a stumbling block to successful AI implementation. The majority of publicly accessible datasets contain fewer than a thousand images. Since the most crucial necessity of automated retinal disease diagnosis is its affordability and extensive screening of the general public, these automated solutions should be capable of performing well in actuality with fundus images captured in everyday practice with little constraints [58]. Despite several publicly available datasets, there remains a scarcity of large, diverse, and accurately annotated datasets, particularly for severe cases like PDR and Macular Edema. One potential solution to this problem is synthesizing data through augmentation techniques, involving fundamental image manipulations such as translation, scaling, rotation, and elastic deformation applied to original training data samples [59].

Generative adversarial networks (GANs) have made breakthroughs in retinal image synthesis in recent years. GANs are built with two models in mind: a generator and a discriminator [60]. The generative model creates realistic images from random noise, while the discriminative model distinguishes between authentic and generated images. The generator tries to deceive the discriminator by producing realistic visuals, and the discriminator strengthens its ability to avoid being misled [61], [62].

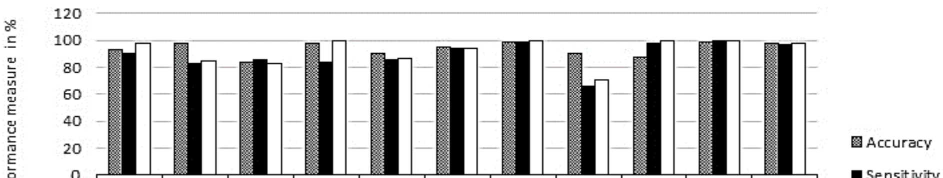
A 2-stage GAN for high-resolution retinal images was introduced by Andreini *et al.* [63]. The suggested model employs a two-step procedure: Primarily, a GAN is trained to provide semantic label maps that describe the vasculature as it grows over time. Second, realistic retinal images are produced from generated vasculature using an image-to-image translation method. In DR patients, the majority of cases are mild or moderate NPDR, with only 5% corresponding to PDR. Due to the scarcity of PDR lesions for model training, Araujo *et al.* [59] introduced a heuristic-based data augmentation approach. They utilized a neo-vessel generation algorithm to synthesize neo-vessel (NV)-like structures. The DRGraduate model for DR grading was trained with this data augmentation technique, and experiments were performed to assess its impact [64]. Chen *et al.* [65] introduced RF-GANs, comprising two generative models, RF-GAN1 and RF-GAN2. RF-GAN1 addresses the domain gap between semantic segmentation datasets and EyePACS. It utilizes HR-Net to enhance high-resolution representation through continuous multi-scale fusion across parallel convolutions, preserving high-resolution features by integrating parallel convolutions from high to low resolution.

7. LIMITATIONS OF EXISTING TECHNIQUES AND FUTURE DIRECTIONS

According to the review conducted in this study, we determine the following areas for further research investigations:

a) Lightweight neural network architectures: While many DL methods for retinal ailments exhibit exceptional performance, their efficiency is often accompanied by high computational resource consumption. Addressing this challenge is crucial to reduce computing requirements without compromising the model's performance.
b) Image synthesis using data augmentation approaches: Another concern arises from the use of small datasets in the evaluation of many techniques. The performance of models on large databases remains uncertain when implemented, compounded by issues of dataset imbalance and limited sample availability. Traditional data augmentation and class balancing techniques are insufficient to address this challenge, highlighting the need for more effective augmentation methods to enhance diagnostic performance.
c) Strengthening generalisability: Most of the systems have to deal with the overhead of pre-processing and post-processing stages. So, effective models need to be developed to standardize techniques in terms of implementation, performance, and accuracy and also to accept retinal images of varying sizes in datasets.
d) Disease-based system rather than lesion-based system: The majority of the existing work we see today is mainly based on DR detection and classification of lesion types. Likewise, there is considerable work on glaucoma detection as well. Works relevant to diseases like retinitis pigmentosa, retinoblastoma, macular hole, retinal tear, retinal detachment, and some other rare syndromes and genetic eye disorders are not explored. So, there is a need to devise disease-based models rather than lesion-based models [46].
e) Integrating deep CNN and active learning framework: To drastically reduce annotation effort, a deep active learning system that integrates fully the CNN model and active learning may be created. Active learning would assist in deciding which images need annotation to acquire outstanding performance with a low budget and quantity of time [66].

Ocular disease diagnosis is evaluated and validated using various performance metrics like Accuracy, Sensitivity, Specificity, F1-Score, and Dice Similarity. Figure 4, depicts the performance evaluation of the various DL techniques. Table 3 (in Appendix) we have summarized various DL approaches, datasets, their performance and shortcomings presented in this study.



	Resnet N/DR [38]	MPSO [24]	Dia Net [35]	Mixed Models[34]	MLCAD[46]	Grad CAM [51]	Vggnet1 6 wbn [37]	Efficient Net B3 [49]	Mask RCNN [76]	ANU Net [74]	Fuzzy based [78]
Accuracy	93,5	97,5	84	98,06	90	95	99,2	90	87,98	98,7	98,2
Sensitivity	90,7	83,15	85,86	83,67	86,1	93,9	98,45	66	97,8	99,7	96,96
Specificity	98,2	84,33	83,06	100	86,8	94,4	100	71	99,6	99,8	98,1

Figure 4. Performance evaluation of DL techniques discussed in this study

8. CONCLUSION

Medical imaging has evolved into a primary tool for clinical and differential diagnosis, with significant advancements. This paper provides a comprehensive summary of diverse DL techniques for ocular disease diagnosis, classification, and segmentation, ranging from traditional ML to advanced methods like CNN, Transfer Learning, Ensemble Learning, and MLC. The discussion includes strategies to address data scarcity, such as augmentation techniques and the use of GANs for generating comparable images. The analysis highlights significant methodological variations in pre-processing, classification, segmentation, and performance evaluation. Notably, most DL methods discussed apply to specific pathological conditions, posing a challenge for universal disease detection in the clinical context.

ACKNOWLEDGEMENTS

We deeply appreciate the support, research assistance, and motivation from JSS Academy of Technology and Engineering, Bengaluru.

APPENDIX

Table 3. Summary of various DL techniques, performance, and shortcomings *(continue)*

Reference	Aim	Technique	Dataset	Performance	Shortcoming
[15]	Contrast Enhancement	Triangular Fuzzy Membership-CLAHE	CASIA-IRIS	Mean Squared Error - 0.0006 Peak-Signal-to-Noise-Ratio -42.2291	The clipping value varies according to the image, the limiting factor is image-dependent
[24]	Contrast Enhancement	CLAHE-MPSO	DRIVE, STARE	Sensitivity-83.15% Specificity-84.33% Accuracy-97.50%	A fixed Scale value of optimization
[67]	Contrast Enhancement	Upgraded CLAHE, TCNN ResNet50	STARE	Sensitivity- 100% Specificity- 100% Accuracy-100%	Only applicable for 5 lesion conditions
[68]	Contrast Enhancement	Fuzzy Clipped CLAHE	MIAS	Peak-signal-to-noise ratio (PSNR)-18.735 Discrete Entropy-5.633	The complex, chosen clip point isn't block adaptive
[35]	Distinguish healthy and diabetic eye	Multi-Stage CNN called Dia-Net	EyePACS, QBB	Accuracy-84% Sensitivity-85.86% Specificity-83.06% F1-Score-84.71%	Cannot distinguish lesions and stages of DR
[33]	MA and Exudates (EX) segmentation	Enhanced residual U-net (ERU-net) with three up-sampling and three down-sampling paths	E-Ophtha, IDRiD, and DDR	Area under the curve (AUC) of 0.9956, 0.9962, 0.9801, for MA and 0.9866, 0.9679, 0.9609 for Ex	Applicable only to MA and EX, other lesion types like hemorrhages could be misclassified
[34]	DR detection and Classification	Mixed models (SVM, BT and KNN) is applied for classification	IDRiD	Accuracy-98.06% Specificity-100% Sensitivity-83.67%	Strong reliance on feature extraction and pre-processing processes.
[69]	DR Grading	CAB for discriminative regions and GAB for global attention features	DDR, Messidor, EyePACS	Accuracy-0.7813, Kappa-0.7699	Challenging to find tiny lesion spots owing to the image supervision level. Can only provide grading scores, not lesion types.
[37]	Pterygium Detection	VggNet16-wbn model with additional batch normalization layers on TL	OPKOM-26, UBIRIS	Accuracy-99.2% Sensitivity-98.45% Specificity-100%	Limited dataset with questionable clinical applicability
[36]	Cataract Detection	GLA-net based on two-level subnets focussing on Global level attention and local-level attention models	9912 retinal fundus images from Beijing Tongren Eye Center	Detection accuracy - 90.65% Grading Accuracy-83.47% Classification Accuracy-81.11%	Extensive supervision is required for detection and grading tasks involving global and local attention models, and limited data availability complicates the problem.
[32]	Glaucoma Diagnosis	EAM-net based on multi-layer average pooling (M-LAP)	ORIGA	Accuracy-0.88 OD segmentation (Dice)-0.9	High-resolution maps are hard to represent. Besides, Optic cup segmentation is completely ignored
[70]	Glaucoma detection (Optic cup (OC) and OD segmentation)	Fuzzy Broad Learning	RIM-ONE-r3, SCRID	DC Score of 0.953,0.856 for OD and OC, and AUC of 0.906 and 0.923	Cannot eliminate noisy images, to accomplish segmentation, individual channels must be extracted.
[71]	Glaucoma Diagnosis	Compactly self-organized Operational Neural Networks (Self -ONNs)	ACRIMA, RIM-ONE, ESOGU	F1 score of 100% 73.9% 93.9% for ESOGU, RIMONE and ACRIMA	Must be tuned and pre-trained for the classification issue.
[72]	Glaucoma Screening	CDeD-Net cup-disc encoder for combined OC and OD segmentation	DRISHTI-GS, RIM-ONE	Sensitivity-95.67%, 99.81% for OC, 97.54%, 99.73% for OD on Drishti, 95.17% and 99.81% for OC, 97.34%,99.73% for OD on RIM-ONE	A large number of unlabelled targets are needed. The model's applicability to diverse datasets is questionable.
[73]	Glaucoma Screening	Five distinct ImageNet trained CNNs as glaucoma classifiers: VGG16,19, ResNet50, InceptionV3, Xception.	ACRIMA	AUC of 0.9605 after optimizing Xception architecture, with a 95.92~97% confidence	Performance worsened when tested on different datasets.

Table 3. Summary of various DL techniques, performance, and shortcomings *(continue)*

Reference	Aim	Technique	Dataset	Performance	Shortcoming
[74]	Multi-class AMD classification (Drusen, Choroidal Neovascularization (CNV))	(ANU-net-FPOA) Atten -tion based U-net, (FPOA) Flower pollination optimization algorithm for hyperparameter tuning. Squeeze-net for classification task	University of California San Diego (UCSD)	Accuracy-98.7% Specificity-99.8% Sensitivity-99.7%	Though the proposed model successfully classified Drusen and CNV, it was unable to classify cases of Macular Edema (DME)
[75]	Retinal Vessel Segmentation	Multi-modal framework ELEMENT with connectivity and region-growing features	DRIVE, STARE, CHASE-DB, IOSTAR, VAMPIRE FA, RC -SLO	Accuracy -97.40% on Drive, 98.27%, 97.78%, 98.34%, 98.04% and 98.35% on STARE, CHASE-DB, VAMPIRE FA, IOSTAR and RC-SLO.	Performs segmentation based on 2D connectivity features, not applicable for 3D Vessel segmentation.
[46]	Pathological changes and diagnosing DR stages	MLCAD system using U-Net based Multilabel SVM and classifier chain	IDRiD, DIARETDB1	Accuracy-95.1%, AUC-91.9%, sensitivity-86.1%, specificity-86.8%, dice score-86.2%	Applicable only for DR and its classification. doesn't work well for other retinal disease
[49]	To identify one or more retinal disorders	Efficient Net model with CNN based multilabel classification	ODIR 2019	Accuracy-0.90, AUC-0.67, F1Score- 0.85, Kappa-0.43	Works well with limited number of datasets, clinical applicability is still an open issue.
[50]	Diagnosis of multiple fundus lesion	Graph neural network - based ML classification to identify eight different types of retinal lesions	7459 fundus images from 2282 patients were used to create a corpus of fundus data	F1 Score -0.808, AUC- 0.986, 0.954, 0.946, 0.957, 0.952, 0.889, 0.937, and 0.926	Model demonstrated a lackluster performance for MA, soft, and hard EX detection
[51]	DR lesion classification and detect lesion region	ML classification including a mechanism for gradient-weighted class activation (Grad-CAM) using ResNet	3228 fundus images were collected	Sensitivity-93.9%, Specificity-94.4%	Ineffective for bright and low-light fundus images don't work for PDR cases
[57]	Identifying multiple and coexisting retinal diseases	A heuristic stacking technique based on multi-label ensemble learning	RFMiD	Accuracy-88.24%	Works well for the RFMiD dataset, but it is uncertain how well it performs with different datasets.
[59]	Synthesis of PDR cases in DR	Heuristic-based Data Augmentation scheme	Messidor-2 Kaggle SCREEN-DR	kappa value-0.78,0.74, 0.70 in SCREEN-DR, Kaggle, Messidor-2	Misclassifies PDR signs with (retinal hemorrhages and fibrosis).
[63]	High-resolution retinal image generation	Two Stage GANS with progressively growing GAN and image translation	DRIVE, CHASE_DB	AUC-98.65%,99.16% Accuracy-96.90%, 97.72% in DRIVE, CHASE	Performance comparison is not convincing due to the varied experimental setups
[65]	Synthesis of DR images	Two generative adversarial models called RFGAN1 and RF-GAN2	EyePACS	Increase in Accuracy-1.53% Kappa-1.70%	Doesn't work well with low-illumination images and the uneven distribution of vessel trees affects image synthesis
[76]	Automatic detection of 39 retinal conditions	Two-level hierarchical system constituting CNNs and Mask-RCNN	249,620 fundus images from various hospitals in China, the US, and databases like Messidor, IDRiD, and Refuge.	F1 score- 0.923, Sensitivity -0.978, Specificity - 0.996 Accuracy-87.98	Weak image segmentation and locality of lesions were not accurately identified
[77]	Segmenting OD for Glaucoma Diagnosis	SL-EACM: Saliency-Level set with enhanced and modified Active Contour Model	CHASE-DB DRION-DB DRISHTI-GS1	Accuracy of 0.994, 0.992, 0.991, and Dice score of 0.979, 0.982, 0.970 on Chase, Drion, and Drishti respectively	The suggested approach failed occasionally with smaller ODs. Relocating the priors would avert this issue
[78]	Detection of DR lesion (Hard exudates)	Exudates detection using binary operation and fuzzy-based classification	DIARETDB0, DIARETDB1	Accuracy-98.2% Specificity-96.96% Sensitivity-98.10%	The model's evaluation, focused on 75 selected DiaretDB0 images for exudate classification, prompts questions about its performance in the presence of other lesions.

REFERENCES

[1] J. D. Steinmetz *et al.*, "Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study," *The Lancet Global Health*, pp. e144–e160, Feb. 2021. doi: 10.1016/S2214-109X(20)30489-7.

[2] Y. Tong, W. Lu, Y. Yu, and Y. Shen, "Application of machine learning in ophthalmic imaging modalities," *Eye and Vision*, vol. 7, no. 1, p. 22, Dec. 2020, doi: 10.1186/s40662-020-00183-6.

[3] S. Muchuchuti and S. Viriri, "Retinal disease detection using deep learning techniques: a comprehensive review," *Journal Imaging*, vol. 9, no. 4, p. 84, Apr. 2023, doi: 10.3390/jimaging9040084.

[4] F. Jiang *et al.*, "Artificial intelligence in healthcare: past, present and future," *Stroke Vasc Neurol*, vol. 2, no. 4, pp. 230–243, Dec. 2017, doi: 10.1136/svn-2017-000101.

[5] S. Majumder and N. Kehtarnavaz, "Multitasking deep learning model for detection of five stages of diabetic retinopathy," *IEEE Access*, vol. 9, pp. 123220–123230, 2021, doi: 10.1109/ACCESS.2021.3109240.

[6] L. Jain, H. V. S. Murthy, C. Patel, and D. Bansal, "Retinal eye disease detection using deep learning," in *2018 Fourteenth International Conference on Information Processing (ICINPRO)*, IEEE, Dec. 2018, pp. 1–6, doi: 10.1109/ICINPRO43533.2018.9096838.

[7] C. Chen, J. H. Chuah, R. Ali, and Y. Wang, "Retinal vessel segmentation using deep learning: A review," *IEEE Access*, vol. 9, pp. 111985–112004, 2021, doi: 10.1109/ACCESS.2021.3102176.

[8] T. Nazir, A. Irtaza, A. Javed, H. Malik, D. Hussain, and R. A. Naqvi, "Retinal image analysis for diabetes-based eye disease detection using deep learning," *Applied Sciences*, vol. 10, no. 18, p. 6185, Sep. 2020, doi: 10.3390/app10186185.

[9] R. Verma, L. Shrinivasan, and B. Hiremath, "Machine learning classifiers for detection of glaucoma," *IAES International Journal of Artificial Intelligence (IJ-AI)*, vol. 12, no. 2, p. 806, Jun. 2023, doi: 10.11591/ijai.v12.i2.pp806-814.

[10] M. I. Razzak, S. Naz, and A. Zaib, "Deep learning for medical image processing: Overview, challenges and the future," *Classification in BioApps: Automation of Decision Making*, 2018, pp. 323–350, doi: 10.1007/978-3-319-65981-7_12.

[11] R. Nuzzi, G. Boscia, P. Marolo, and F. Ricardi, "The impact of artificial intelligence and deep learning in eye diseases: A review," *Front Med (Lausanne)*, vol. 8, Aug. 2021, doi: 10.3389/fmed.2021.710329.

[12] C. Swathi, B. K. Anoop, D. A. S. Dhas, and S. P. Sanker, "Comparison of different image preprocessing methods used for retinal fundus images," in *Conference on Emerging Devices and Smart Systems (ICEDSS)*, 2017, pp. 175–179, doi: 10.1109/ICEDSS.2017.8073677.

[13] S. P. Mary and V. Thanikaiselvan, "Unified adaptive framework for contrast enhancement of blood vessels," *International Journal of Electrical and Computer Engineering (IJECE)*, vol. 10, no. 1, p. 767, Feb. 2020, doi: 10.11591/ijece.v10i1.pp767-777.

[14] S. M. Pizer *et al.*, "Adaptive histogram equalization and its variations," *Comput Vis Graph Image Process*, vol. 39, no. 3, pp. 355–368, Sep. 1987, doi: 10.1016/S0734-189X(87)80186-X.

[15] B. S. Vidya and E. Chandra, "Triangular fuzzy membership-contrast limited adaptive histogram equalization (TFM-CLAHE) for enhancement of multimodal biometric images," *Wirel Pers Communication*, vol. 106, no. 2, pp. 651–680, May 2019, doi: 10.1007/s11277-019-06184-6.

[16] I. Qureshi, J. Ma, and K. Shaheed, "A hybrid proposed fundus image enhancement framework for diabetic retinopathy," *Algorithms*, vol. 12, no. 1, p. 14, Jan. 2019, doi: 10.3390/a12010014.

[17] A. W. Setiawan, T. R. Mengko, O. S. Santoso, and A. B. Suksmono, "Color retinal image enhancement using CLAHE," in *International Conference on ICT for Smart Society*, IEEE, Jun. 2013, pp. 1–3, doi: 10.1109/ICTSS.2013.6588092.

[18] A. F. Khan, A. Jalil, I. U. Haq, and S. I. H. Shah, "Automatic localization of macula and identification of macular degeneration in retinal fundus images," in *2021 International Conference on Electrical, Communication, and Computer Engineering (ICECCE)*, IEEE, Jun. 2021, pp. 1–6, doi: 10.1109/ICECCE52056.2021.9514083.

[19] Y. Elloumi, M. Akil, and N. Kehtarnavaz, "A mobile computer aided system for optic nerve head detection," *Comput Methods Programs Biomed*, vol. 162, pp. 139–148, Aug. 2018, doi: 10.1016/j.cmpb.2018.05.004.

[20] T. Lestari and A. Luthfi, "Retinal blood vessel segmentation using gaussian filter," *In Journal of physics: conference series*, vol. 1376, no. 1, p. 012023, Nov. 2019, doi: 10.1088/1742-6596/1376/1/012023.

[21] K. B. Khan, A. A. Khaliq, A. Jalil, and M. Shahid, "A robust technique based on VLM and Frangi filter for retinal vessel extraction and denoising," *PLoS One*, vol. 13, no. 2, p. e0192203, Feb. 2018, doi: 10.1371/journal.pone.0192203.

[22] S. Sahu, A. K. Singh, S. P. Ghrera, and M. Elhoseny, "An approach for de-noising and contrast enhancement of retinal fundus image using CLAHE," *Opt Laser Technologi*, vol. 110, pp. 87–98, Feb. 2019, doi: 10.1016/j.optlastec.2018.06.061.

[23] K. Li, X. Qi, Y. Luo, Z. Yao, X. Zhou, and M. Sun, "Accurate retinal vessel segmentation in color fundus images via fully attention-based networks," *IEEE Journal Biomed Health Information*, vol. 25, no. 6, pp. 2071–2081, Jun. 2021, doi: 10.1109/JBHI.2020.3028180.

[24] K. Aurangzeb, S. Aslam, M. Alhussein, R. A. Naqvi, M. Arsalan, and S. I. Haider, "Contrast enhancement of fundus images by employing modified PSO for improving the performance of deep learning models," *IEEE Access*, vol. 9, pp. 47930–47945, 2021, doi: 10.1109/ACCESS.2021.3068477.

[25] B. Bhatkalkar, A. Joshi, S. Prabhu, and S. Bhandary, "Automated fundus image quality assessment and segmentation of optic disc using convolutional neural networks," *International Journal of Electrical and Computer Engineering (IJECE)*, vol. 10, no. 1, p. 816, Feb. 2020, doi: 10.11591/ijece.v10i1.pp816-827.

[26] A. Naizagarayeva *et al.*, "Detection of heart pathology using deep learning methods," *International Journal of Electrical and Computer Engineering (IJECE)*, vol. 13, no. 6, p. 6673, Dec. 2023, doi: 10.11591/ijece.v13i6.pp6673-6680.

[27] R. H. Hridoy, A. D. Arni, and A. Haque, "Improved vision-based diagnosis of multi-plant disease using an ensemble of deep learning methods," *International Journal of Electrical and Computer Engineering (IJECE)*, vol. 13, no. 5, p. 5109, Oct. 2023, doi: 10.11591/ijece.v13i5.pp5109-5117.

[28] S. S. Reddy, V. V. S. Rama Raju, C. R. Swaroop, and N. Pilli, "Evaluation of deep learning models for melanoma image classification," *International Journal of Public Health Science (IJPHS)*, vol. 12, no. 3, p. 1189, Sep. 2023, doi: 10.11591/ijphs.v12i3.22983.

[29] S. K. Venkatapathiah, S. S. Selvan, P. Nanda, M. Shetty, V. M. Swamy, and K. Awasthi, "Deep learning based object detection in nailfold capillary images," *IAES International Journal of Artificial Intelligence (IJ-AI)*, vol. 12, no. 2, p. 931, Jun. 2023, doi: 10.11591/ijai.v12.i2.pp931-942.

[30] A. P. Begum and P. Selvaraj, "Alzheimer's disease classification and detection by using AD-3D DCNN model," *Bulletin of Electrical Engineering and Informatics (BEEI)*, vol. 12, no. 2, pp. 882–890, Dec. 2022, doi: 10.11591/eei.v12i2.4446.

[31] M. Jayaram, G. Kalpana, S. R. Borra, and B. D. Bhavani, "A brief study on rice diseases recognition and image classification: fusion deep belief network and S-particle swarm optimization algorithm," *International Journal of Electrical and Computer Engineering (IJECE)*, vol. 13, no. 6, p. 6302, Dec. 2023, doi: 10.11591/ijece.v13i6.pp6302-6311.

[32] W. Liao, B. Zou, R. Zhao, Y. Chen, Z. He, and M. Zhou, "Clinical interpretable deep learning model for glaucoma diagnosis," *IEEE Journal Biomed Health Information*, vol. 24, no. 5, pp. 1405–1412, May 2020, doi: 10.1109/JBHI.2019.2949075.

[33] C. Kou, W. Li, Z. Yu, and L. Yuan, "An enhanced residual U-Net for microaneurysms and exudates segmentation in fundus images," *IEEE Access*, vol. 8, pp. 185514–185525, 2020, doi: 10.1109/ACCESS.2020.3029117.

[34] A. Bilal, G. Sun, Y. Li, S. Mazhar, and A. Q. Khan, "Diabetic retinopathy detection and classification using mixed models for a disease grading database," *IEEE Access*, vol. 9, pp. 23544–23553, 2021, doi: 10.1109/ACCESS.2021.3056186.

[35] M. T. Islam, H. R. H. Al-Absi, E. A. Ruagh, and T. Alam, "DiaNet: A deep learning based architecture to diagnose diabetes using retinal images only," *IEEE Access*, vol. 9, pp. 15686–15695, 2021, doi: 10.1109/ACCESS.2021.3052477.

[36] X. Xu *et al.*, "GLA-Net: A global-local attention network for automatic cataract classification," *Journal Biomed Information*, vol. 124, p. 103939, Dec. 2021, doi: 10.1016/j.jbi.2021.103939.

[37] N. S. M. Zamani, W. M. D. W. Zaki, A. B. Huddin, A. Hussain, H. A. Mutalib, and A. Ali, "Automated pterygium detection using deep neural network," *IEEE Access*, vol. 8, pp. 191659–191672, 2020, doi: 10.1109/ACCESS.2020.3030787.

[38] N. M. Al-Moosawi and R. S. Khudeyer, "ResNet-n/DR: Automated diagnosis of diabetic retinopathy using a residual neural network," *TELKOMNIKA (Telecommunication Computing Electronics and Control)*, vol. 21, no. 5, p. 1051, Oct. 2023, doi: 10.12928/telkomnika.v21i5.24515.

[39] C. Tan, F. Sun, T. Kong, W. Zhang, C. Yang, and C. Liu, "A survey on deep transfer learning," *In Artificial Neural Networks and Machine Learning–ICANN 2018: 27th International Conference on Artificial Neural Networks, Rhodes, Greece, October 4-7, 2018, Proceedings*, 2018, pp. 270–279. doi: 10.1007/978-3-030-01424-7_27.

[40] H.-C. Shin *et al.*, "Deep convolutional neural networks for computer-aided detection: CNN architectures, dataset characteristics and transfer learning," *IEEE Trans Med Imaging*, vol. 35, no. 5, pp. 1285–1298, May 2016, doi: 10.1109/TMI.2016.2528162.

[41] N. A. Baker, N. Zengeler, and U. Handmann, "A transfer learning evaluation of deep neural networks for image classification," *Mach Learn Knowl Extr*, vol. 4, no. 1, pp. 22–41, Jan. 2022, doi: 10.3390/make4010002.

[42] J. P. Gujjar, H. R. P. Kumar, and N. N. Chiplunkar, "Image classification and prediction using transfer learning in colab notebook," *Global Transitions Proceedings*, vol. 2, no. 2, pp. 382–385, Nov. 2021, doi: 10.1016/j.gltp.2021.08.068.

[43] P. Ganchev, D. Malehorn, W. L. Bigbee, and V. Gopalakrishnan, "Transfer learning of classification rules for biomarker discovery and verification from molecular profiling studies," *Journal Biomed Information*, vol. 44, pp. S17–S23, Dec. 2011, doi: 10.1016/j.jbi.2011.04.009.

[44] M. K. Jabbar, J. Yan, H. Xu, Z. U. Rehman, and A. Jabbar, "Transfer learning-based model for diabetic retinopathy diagnosis using retinal images," *Brain Science*, vol. 12, no. 5, p. 535, Apr. 2022, doi: 10.3390/brainsci12050535.

[45] M. Alghamdi and M. Abdel-Mottaleb, "A comparative study of deep learning models for diagnosing glaucoma from fundus images," *IEEE Access*, vol. 9, pp. 23894–23906, 2021, doi: 10.1109/ACCESS.2021.3056641.

[46] E. Abdelmaksoud, S. El-Sappagh, S. Barakat, T. Abuhmed, and M. Elmogy, "Automatic diabetic retinopathy grading system based on detecting multiple retinal lesions," *IEEE Access*, vol. 9, pp. 15939–15960, 2021, doi: 10.1109/ACCESS.2021.3052870.

[47] H. Fu, J. Cheng, Y. Xu, D. W. K. Wong, J. Liu, and X. Cao, "Joint optic disc and cup segmentation based on multi-label deep network and polar transformation," *IEEE Trans Med Imaging*, vol. 37, no. 7, pp. 1597–1605, Jul. 2018, doi: 10.1109/TMI.2018.2791488.

[48] J. Lin, Q. Cai, and M. Lin, "Multi-label classification of fundus images with graph convolutional network and self-supervised learning," *IEEE Signal Process Lett*, vol. 28, pp. 454–458, 2021, doi: 10.1109/LSP.2021.3057548.

[49] J. Wang, L. Yang, Z. Huo, W. He, and J. Luo, "Multi-label classification of fundus images with efficientNet," *IEEE Access*, vol. 8, pp. 212499–212508, 2020, doi: 10.1109/ACCESS.2020.3040275.

[50] Y. Cheng, M. Ma, X. Li, and Y. Zhou, "Multi-label classification of fundus images based on graph convolutional network," *BMC Medical Informatics and Decision Making*, vol. 21, no. S2, p. 82, Jul. 2021, doi: 10.1186/s12911-021-01424-x.

[51] H. Jiang *et al.*, "A multi-label deep learning model with interpretable Grad-CAM for diabetic retinopathy classification," in *2020 42nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, IEEE, Jul. 2020, pp. 1560–1563, doi: 10.1109/EMBC44109.2020.9175884.

[52] H. Q. Gheni and W. L. Al-Yaseen, "Using ensemble techniques based on machine and deep learning for solving intrusion detection problems: A survey," *Karbala International Journal of Modern Science*, vol. 9, no. 1, Jan. 2023, doi: 10.33640/2405-609X.3277.

[53] Md. M. H. Sabbir, A. Sayeed, and Md. A.-U.-Z. Jamee, "Diabetic retinopathy detection using texture features and ensemble learning," in *2020 IEEE Region 10 Symposium (TENSYMP)*, IEEE, 2020, pp. 178–181, doi: 10.1109/TENSYMP50017.2020.9230600.

[54] A. Mohammed and R. Kora, "A comprehensive review on ensemble deep learning: Opportunities and challenges,"*Journal of King Saud University-Computer and Information Sciences*, vol. 35, no. 2, pp. 757–774, Feb. 2023, doi: 10.1016/j.jksuci.2023.01.014.

[55] E. Ho *et al.*, "Deep ensemble learning for retinal image classification," *Translational Vision Science and Technology*, vol. 11, no. 10, p. 39, Oct. 2022, doi: 10.1167/tvst.11.10.39.

[56] S. Qummar *et al.*, "A deep learning ensemble approach for diabetic retinopathy detection," *IEEE Access*, vol. 7, pp. 150530–150539, 2019, doi: 10.1109/ACCESS.2019.2947484.

[57] L. Lyu, I. E. Toubal, and K. Palaniappan, "Multi-expert deep networks for multi-disease detection in retinal fundus images," in *2022 44th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, IEEE, Jul. 2022, pp. 1818–1822, doi: 10.1109/EMBC48229.2022.9871762.

[58] M. N. Bajwa, G. A. P. Singh, W. Neumeier, M. I. Malik, A. Dengel, and S. Ahmed, "G1020: A benchmark retinal fundus image dataset for computer-aided glaucoma detection," in *2020 International Joint Conference on Neural Networks (IJCNN)*, IEEE, Jul. 2020, pp. 1–7, doi: 10.1109/IJCNN48605.2020.9207664.

[59] T. Araujo *et al.*, "Data augmentation for improving proliferative diabetic retinopathy detection in eye fundus images," *IEEE Access*, vol. 8, pp. 182462–182474, 2020, doi: 10.1109/ACCESS.2020.3028960.

[60] G. Lim, P. Thombre, M. L. Lee, and W. Hsu, "Generative data augmentation for diabetic retinopathy classification," in *2020 IEEE 32nd International Conference on Tools with Artificial Intelligence (ICTAI)*, 2020, pp. 1096–1103, doi: 10.1109/ICTAI50040.2020.00167.

[61] V. Bellemo, P. Burlina, L. Yong, T. Y. Wong, and D. S. W. Ting, "Generative adversarial networks (GANs) for retinal fundus image synthesis," *In Computer Vision–ACCV 2018 Workshops: 14th Asian Conference on Computer Vision, Perth, Australia, December 2–6, 2018, Revised Selected Papers*, 2019, pp. 289–302, doi: 10.1007/978-3-030-21074-8_24.

[62] I. Goodfellow *et al.*, "Generative adversarial networks," *Commun ACM*, vol. 63, no. 11, pp. 139–144, Oct. 2020, doi: 10.1145/3422622.

[63] P. Andreini *et al.*, "A two-stage GAN for high-resolution retinal image generation and segmentation," *Electronics (Basel)*, vol. 11, no. 1, p. 60, Dec. 2021, doi: 10.3390/electronics11010060.

[64] T. Araújo *et al.*, "DR|GRADUATE: Uncertainty-aware deep learning-based diabetic retinopathy grading in eye fundus images," *Medical Image Analysis*, vol. 63, p. 101715, Jul. 2020, doi: 10.1016/j.media.2020.101715.

[65] Y. Chen, J. Long, and J. Guo, "RF-GANs: A method to synthesize retinal fundus images based on generative adversarial network," *Computational Intelligence and Neuroscience*, vol. 2021, pp. 1–17, Nov. 2021, doi: 10.1155/2021/3812865.

[66] J. Wu *et al.*, "Multi-label active learning algorithms for image classification," *ACM computing surveys*, vol. 53, no. 2, pp. 1–35, Mar. 2021, doi: 10.1145/3379504.

[67] S. S. M. Sheet, T.-S. Tan, M. A. As'ari, W. H. W. Hitam, and J. S. Y. Sia, "Retinal disease identification using upgraded CLAHE filter and transfer convolution neural network," *ICT Express*, vol. 8, no. 1, pp. 142–150, Mar. 2022, doi: 10.1016/j.icte.2021.05.002.
[68] S. Jenifer, S. Parasuraman, and A. Kadirvelu, "Contrast enhancement and brightness preserving of digital mammograms using fuzzy clipped contrast-limited adaptive histogram equalization algorithm," *Applied Soft Computing*, vol. 42, pp. 167–177, May 2016, doi: 10.1016/j.asoc.2016.01.039.
[69] A. He, T. Li, N. Li, K. Wang, and H. Fu, "CABNet: Category attention block for imbalanced diabetic retinopathy grading," *IEEE Applied Soft Computing*, vol. 40, no. 1, pp. 143–153, Jan. 2021, doi: 10.1109/TMI.2020.3023463.
[70] R. Ali *et al.*, "Optic disk and cup segmentation through fuzzy broad learning system for glaucoma screening," *IEEE Transactions on Industrial Informatics*, vol. 17, no. 4, pp. 2476–2487, Apr. 2021, doi: 10.1109/TII.2020.3000204.
[71] O. C. Devecioglu, J. Malik, T. Ince, S. Kiranyaz, E. Atalay, and M. Gabbouj, "Real-time glaucoma detection from digital fundus images using self-ONNs," *IEEE Access*, vol. 9, pp. 140031–140041, 2021, doi: 10.1109/ACCESS.2021.3118102.
[72] M. Tabassum *et al.*, "CDED-Net: Joint segmentation of optic disc and optic cup for glaucoma screening," *IEEE Access*, vol. 8, pp. 102733–102747, 2020, doi: 10.1109/ACCESS.2020.2998635.
[73] A. Diaz-Pinto, S. Morales, V. Naranjo, T. Köhler, J. M. Mossi, and A. Navea, "CNNs for automatic glaucoma assessment using fundus images: an extensive validation," *Biomed Eng Online*, vol. 18, no. 1, p. 29, Dec. 2019, doi: 10.1186/s12938-019-0649-y.
[74] G. M. Nagamani and T. Sudhakar, "Automated classification of age-related macular degeneration from optical coherence tomography images using deep learning approach," *IAES International Journal of Artificial Intelligence (IJ-AI)*, vol. 12, no. 4, p. 2011, Dec. 2023, doi: 10.11591/ijai.v12.i4.pp2011-2021.
[75] E. O. Rodrigues, A. Conci, and P. Liatsis, "ELEMENT: Multi-modal retinal vessel segmentation based on a coupled region growing and machine learning approach," *IEEE Journal Biomed Health Inform*, vol. 24, no. 12, pp. 3507–3519, Dec. 2020, doi: 10.1109/JBHI.2020.2999257.
[76] L.-P. Cen *et al.*, "Automatic detection of 39 fundus diseases and conditions in retinal photographs using deep neural networks," *Nature Communications*, vol. 12, no. 1, p. 4828, Aug. 2021, doi: 10.1038/s41467-021-25138-w.
[77] S. Naz and K. A. R. Rao, "Segmentation of optic disc in retinal images for glaucoma diagnosis by saliency level set with enhanced active contour model," *International Journal of Electrical and Computer Engineering (IJECE)*, vol. 13, no. 3, p. 2801, Jun. 2023, doi: 10.11591/ijece.v13i3.pp2801-2811.
[78] A. Pradeep and X. F. Joseph, "Binary operation based hard exudate detection and fuzzy based classification in diabetic retinal fundus images for real time diagnosis applications," *International Journal of Electrical and Computer Engineering (IJECE)*, vol. 10, no. 3, p. 2305, Jun. 2020, doi: 10.11591/ijece.v10i3.pp2305-2312.

BIOGRAPHIES OF AUTHORS

Rajatha holds a Bachelor's in Information Science and Engineering from Canara Engineering College, Mangalore, and a Master's in Computer Science and Engineering from Shri Devi Institute of Technology and Engineering, Mangalore. Currently pursuing a Ph.D. at JSSATE, Bengaluru, she works as an Assistant Professor in the Department of Computer Science and Engineering, SJBIT, Bengaluru. Her research interests encompass computer vision, image processing, medical image analysis, machine learning, and deep learning. She can be contacted at email: rajathabhatkaje@gmail.com.

Dr. D. V. Ashoka currently a Professor in the Information Science and Engineering department at JSS Academy of Technical Education, Bangalore, he previously served as Dean (Research) at JSSATEB and held leadership roles in CSE/ISE departments at reputable engineering colleges in Karnataka, India. He specializes in Knowledge Engineering, Operating System Virtualization, Requirement Engineering, Artificial Intelligence, Software Engineering, and Architecture. He has supervised over ten completed and ongoing PhDs. Additionally, he chairs the Board of Examiners at VTU, Belagavi, and actively contributes to various educational committees in India. Recognized with the National Award "Rashtriya Ekta Samman-2013," he is listed in Who's Who in the World 2011-12 by Marquis Who's Who. He can be contacted at email: dr.dvashoka@gmail.com.